## **SLEEP, NAPS AND HEALTH RISK**

# Daily Siesta, Cardiovascular Risk Factors, and Measures of Subclinical Atherosclerosis: Results of the Heinz Nixdorf Recall Study

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**Background:** Several studies have assessed the association between siesta and cardiovascular outcomes. Concern exists that confounding might have distorted these results and contributed to discrepancies among them. This report examines the association between siesta habits and cardiovascular risk factors, including sleep disturbances at night, depressed mood, and measures of subclinical atherosclerosis such as coronary calcium score and ankle brachial index.

**Methods:** The baseline examination of 4,797 participants aged 45-74 years included interviews, physical examinations, laboratory tests, and electron beam computed tomography. We compared the baseline prevalence of depressed mood, nighttime sleep disturbances, and health status in 3 categories of siesta habits: irregular or no siestas; daily short siestas (1 hour or less); and daily long siestas (>1 hour). We also characterized cardiovascular risk factor distributions in the 3 siesta groups and conducted a sensitivity analysis of the potential for confounding by these factors in studies of incident cardiovascular disease.

Results: Depressed mood and poor self-perceived health status at base-

line had positive associations with the age-standardized prevalence of daily long siestas among both men and women. Daily takers of long siestas had a considerably higher prevalence of cardiovascular risk factors in both sexes and appreciably worse measures of subclinical atherosclerosis in men only, in comparison with either of the other siesta groups. Daily long siestas had positive associations with prevalence of several cardiovascular risk factors and measures of subclinical atherosclerosis.

**Conclusions:** If uncontrolled, these associations could produce appreciable confounding in studies of siesta habits and incidence of cardiovascular events.

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## INTRODUCTION

ALTHOUGH SIESTA (AFTERNOON OR MIDDAY NAP) IS A COMMON TRADITION IN MEDITERRANEAN REGIONS, SURVEYS HAVE SHOWN IT TO BE A PREVALENT feature of adult sleep-wake activity in other locales as well, including

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the United States, Australia, Nigeria, and the United Kingdom.<sup>1</sup> Several studies, mainly in Mediterranean populations, have examined associations between siestas and health outcomes, including myocardial infarction, stroke, and overall mortality. Two case-control studies in Greece reported inverse associations between the duration of siestas and the incidence of myocardial infarction without specifying the regularity of midday napping.<sup>2,3</sup> A case-control study in Costa Rica, in contrast, reported a positive association, especially for daily siestas lasting longer than 1 hour.4 Two cohort studies in Israel reported positive associations of daily siestas with cardiovascular mortality,5,6 one suggesting stronger associations among men for longer siestas and stronger associations among women for shorter siestas.<sup>6</sup> A recent Greek cohort study showed a protective effect of regular and occasional siesta (defined as at least 3 siestas per week) on the coronary mortality among men only.7

These associations may have been distorted by confounding by unmeasured or poorly measured cardiovascular risk factors, 6 sleep apnea (which is related to arterial hypertension and obesity8), and sleep disturbances at night. Consequently, one would expect to observe a higher prevalence of cardiovascular risk factors and nocturnal sleep disturbances among persons who take siestas.

Neither the prevalence of siesta habits nor associations among siesta habits, nocturnal habits, disturbances of sleep, and cardio-vascular risk factors have been well characterized in northern European populations to date. In Germany, population-based prevalence estimates of nocturnal sleep disturbances are scant. 9-11 In addition, information appears to be unavailable for any popula-

tion on the association between siesta habits and measures of subclinical atherosclerosis, including ankle brachial index (ABI) and coronary calcification as measured by electron beam computed tomography (EBT).

We present results of a cross-sectional analysis of results from the baseline examinations in the ongoing Heinz Nixdorf Recall Study, a population-based prospective cohort study of the comparative predictive value of modern risk stratification techniques for coronary events. <sup>12,13</sup> Our aims are to describe the prevalence of siesta habits in this population; to examine the associations of these habits with the baseline prevalence of depressed mood, nocturnal sleep disturbances, and self-perceived health status; and to assess the potential for confounding by cardiovascular risk factors, including subclinical atherosclerosis measures, in prospective studies relating baseline siesta habits to the incidence of cardiovascular events.

### **MATERIAL AND METHODS**

The rationale, design and methods of the Heinz Nixdorf Recall Study have been described in detail. <sup>12,13</sup> Briefly, from December 2000 through August 2003, we recruited 4,814 participants, aged 45-75 years, residing in the industrial cities Essen, Bochum, and Mülheim, in the Ruhr area of Germany. Participants were drawn from mandatory residence lists, with a response rate of 56 percent. The participants are currently under follow-up until July 2008.

The baseline examinations included interviews for cardiovascular risk factors; anthropometric measurements such as height, weight, waist-to-hip ratio, blood pressure, and ankle brachial index (ABI); comprehensive laboratory tests of blood and urine; resting and exercise electrocardiograms; and electron beam computed tomography (EBT) to assess coronary calcium quantities.<sup>13</sup> The study organization was certified according to DIN EN ISO9001:2000.<sup>14</sup>

Participants on antihypertensive medication or with systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg¹⁵ were defined as hypertensive. Participants were classified as having diabetes if they reported a history of diagnosis of the disease, took antidiabetic drugs, or had a nonfasting glucose level ≥200 mg/dL. Participants with a self-reported history of coronary artery disease (myocardial infarction, revascularization of coronary arteries including balloon dilatation, and coronary bypass surgery) were defined as having manifest CAD.

We defined the presence of relevant coronary calcium as an Agatston score<sup>16</sup> of 100 or higher.<sup>17,18</sup> We considered high-sensitive C-reactive protein (CRP) concentrations >3 mg/L as elevated values.<sup>19</sup> ABI <0.9 was considered abnormal.<sup>20</sup> Dyslipidemia was defined as either a total cholesterol ≥240 mg/dL, a HDL cholesterol <40 mg/dL, or intake of lipid lowering drugs.<sup>21</sup> Obesity was defined as a body mass index (BMI) ≥30 kg/m². An increased waist circumference was defined as >102 cm among men and >88 cm among women.<sup>21</sup>

The interview on sleep habits included several questions on sleep duration, frequency and duration of siesta, and nocturnal sleep disturbances during the 4 weeks before interview: difficulty falling asleep (DFA), difficulty maintaining sleep (DMS), early morning arousal (EMA) during the 4 weeks before interview, and frequency and duration of siestas. We defined nocturnal sleep durations <6 hours as excessively short and durations >8 hours as excessively long.<sup>22-26</sup>

Frequency of nocturnal sleep disturbances was assessed as never, sometimes (one or fewer per week), frequently (at least twice per week), and nearly every night. We defined persons having prevalent nocturnal sleep disturbances if they occurred nearly every night.<sup>26</sup> The frequency categories for siesta were never, <1 per week, 1-4 per week, 5-6 per week, and daily. We defined siestas taken ≥5 days per week as daily siestas and siestas taken less often as irregular.<sup>6,27</sup> The latter group was combined with those reporting no siestas, as the cardiovascular risk factor prevalence was virtually identical in these groups. All participants who reported siestas reported sleeping at night.

We assessed depressed mood with the Center for Epidemiologic Studies-Depression (CES-D) scale.<sup>28,29</sup> We modified the CES-D by excluding the symptom "my sleep was restless" to remove the item's correlation with questions on sleep disturbances or siesta frequency.<sup>30</sup> Thus, the scale had 14 items and a range of 0-42.

The question on self-perceived health status in the recent 12 months had an ordinal scale: very good, good, satisfactory, less well, poor. Participants who rated their health as less well or poor were regarded as having reduced self-perceived health status.

## **Statistical Methods**

Of the 4,472 non-CAD subjects aged 45-74 years, 4% had not undergone EBT scanning and 2% had missing data on ABI. All other risk factors included in the analyses had missing values of less than 1%. We calculated sex-specific and age-specific (45-54 y, 55-64 y, and 65-74 y) prevalence estimates of siesta habits and nocturnal sleep disturbances. We calculated the average overall sleep duration per day as hours of sleep per week divided by 7. To classify participants without CAD with regard to depressed mood, we used the sex-specific 90th percentiles (men: ≥13, women: ≥17) of the modified score.

We calculated age-standardized prevalences with the age distribution of the overall non-CAD group as the standard (13% aged 45-49 years, 19% aged 50-54 years, 18% aged 55-59 years, 22% aged 60-64 years, 16% aged 65-69 years, 11% aged 70-74 years). For the comparison of subjects taking daily siestas >1 hour in length with those never or irregularly taking siestas, or taking daily short siestas, we calculated sex-specific age-standardized prevalence ratios and 95% confidence intervals, with people taking no or irregular siestas serving as the reference group.

To quantify the presence of CAD risk factors, we created a count variable for the number of established risk factors at baseline for each person in the non-CAD group. Ten risk factors were included in this count: age (≥60 years), smoking, diabetes mellitus, hypertension, dyslipidemia, obesity, increased waist circumference, increased CRP, increased coronary calcium score, and abnormal ABI according to the definitions given above. We used these counts in a sensitivity analysis to assess the potential for confounding by CAD risk factors in prospective studies of baseline siesta in relation to incident CAD.

Starting with a 10-year CAD risk of 0.02 from the Framingham prediction model for persons aged 53 years with no Framingham risk factors, we used the exponential formula,  $R = 1 - \exp(-It)$  (where R is the 10-year risk, I is the incidence rate and t=10 years) to convert this risk to a baseline rate of 20.3 CAD cases per 10,000 person-years. For simplification, we assumed that siesta has no effect on the CAD incidence rate and that each potentially confounding risk factor has the same rate ratio,

**Table 1**—Sleep Characteristics and Sleep Disturbances Among 4,472 Men and Women of the Heinz Nixdorf Recall Study, Aged 45-74 Years, With No History of Coronary Artery Disease

		Sleep Duration at Night			Sleep Disturbances nearly every night (%) <sup>a</sup> Daily Sies						Average Overall Sleep Duration (night & siesta) <sup>b</sup>	
	N	Median (min)	<6h/ night (%)	>8h/ night (%)	DFA	DMS	EMA	Any (%)	>1h/day (%)	Median (min) <sup>c</sup>	Median (min)	
Men			(,,,)	(,,,)								
All (crude)	2132	420	10.6	6.9	7.0	32.3	8.1	16.7	3.1	60	422	
All (age-stand.	)		9.9	6.5	6.5	30.4	7.5	15.8	2.9			
45-54 yrs	707	420	12.7	3.4	6.6	16.3	6.7	7.4	1.3	45	420	
55-64 yrs	852	420	11.5	6.9	8.4	35.4	10.2	15.4	3.2	60	424	
65-74 yrs	573	420	6.8	11.2	5.6	47.5	6.7	30.1	5.1	60	460	
Women												
All (crude)	2340	420	15.5	7.1	11.7	38.7	12.2	15.1	1.9	30	420	
All (age-stand.	)		14.4	6.6	10.9	36.0	11.3	14.0	1.7			
45-54 yrs	743	420	14.3	2.7	10.0	28.1	11.3	6.2	1.2	45	420	
55-64 yrs	933	420	15.6	8.7	11.9	42.6	12.2	13.9	1.2	30	420	
65-74 yrs	664	420	16.6	9.7	13.5	45.2	13.1	26.9	3.6	45	429	

<sup>&</sup>lt;sup>a</sup>DFA: difficulties falling asleep; DMS: difficulties maintaining sleep; EMA: early morning arousal

which we specified as 1.3, 1.5, 1.7, and 2.0 in separate analyses. We additionally assumed constancy of each risk factor's rate ratio within strata of all the other risk factors. This mirrors the routine assumption when potential confounders are specified only as main effects, without product interactions among them, in multiple regression models. Thus, in the analysis in which the risk factors were assumed to have a rate ratio of 1.5, the rate ratio contrasting persons with 5 of the 10 risk factors to those with none was  $1.5^5 = 7.6$ .

In the first sensitivity analysis, we assumed adjustment for none of the risk factors (i.e., a crude analysis). In the second analysis, we assumed adjustment for age and removed age from the count variable, thereby reducing the theoretical maximum for this variable to 9. In the third analysis, we assumed adjustment for age and smoking, removed age and smoking from the count variable, and reduced the theoretical maximum to 8. We then added hypertension, diabetes and waist circumference to the fourth, fifth, and sixth analyses, respectively, in a similar fashion. From the observed distributions of the risk factor count variable, we were thus able to project hypothetical CAD rates for each of the 3 siesta groups. Under the assumption of no siesta effect on CAD, the rate ratios obtained from these hypothetical rates provide an approximate indication of the direction and magnitude of potential confounding.

## **RESULTS**

Overall, 325 subjects aged 45-74 years (7%) had a history of CAD. Table 1 presents sleep characteristics of participants without a history of CAD. The median sleep duration at night did not vary by age and sex, but elderly women more often tended to sleep <6 hours per night than elderly men. The prevalence of all nocturnal sleep disturbances was considerably higher among women than among men, regardless of age. The most frequently

reported regular sleep disturbance among men and women was difficulty maintaining asleep at night among both. The prevalence of the 3 major types of nocturnal sleep disturbances increased monotonically with age among women. The prevalence of daily siesta was slightly higher among men than women, regardless of age. The median duration of siesta among daily siesta takers was particularly long in older men, among whom siestas contributed appreciably to the total daily sleep duration.

Table 2 presents the sleep characteristics of the 325 participants with a history of CAD. Because only 68 women had manifest CAD, age-specific estimates of sleep characteristics in that group are not shown. Women with CAD had a considerably higher prevalence of excessively short sleep durations (<6 h) than men with CAD. Difficulty falling asleep and early morning arousal were more prevalent among women than men, whereas the prevalence of difficulty maintaining sleep was about the same in the 2 sexes. Generally, prevalence of siesta and of nocturnal sleep disturbances were higher among participants who had CAD than among those who did not.

Poor self-perceived health status, depressive mood, difficulties falling asleep, and excessively short nocturnal sleep durations were positively associated with daily long siestas among both men and women. Early morning awakening was negatively associated with regular siesta among men and positively associated with regular siesta among women (Table 3).

Participants taking short daily siestas showed prevalence of CAD risk factors similar to those of participants who took siestas no more than occasionally (Table 4). Participants taking daily long siestas, however, showed higher prevalence of CAD risk factors, and, especially in men, higher prevalence of subclinical atherosclerosis as measured by ABI and EBT. The overall number of established CAD risk factors was higher among subjects taking daily long siestas compared with subjects taking daily short siestas, irregular siestas, or no siestas.

<sup>&</sup>lt;sup>b</sup>Overall sleep duration including sleep at night and siesta of any frequency per week

<sup>&</sup>lt;sup>c</sup>Median duration of siesta (minutes) among subjects with daily siesta

Missing data: per Item < 1%, therefore missing data were excluded.

Table 2—Sleep Characteristics and Sleep Disturbances Among 325 Men and Women of the Heinz Nixdorf Recall Study, Aged 45-74 Years, With a History of Coronary Artery Disease

	Sleep	Duration	at Night	Sleep Disturbances nearly every night (%) <sup>a</sup>			Daily Siesta			Average Overall Sleep Duration (night & siesta) <sup>b</sup>	
N	Median (min)	<6h/ night (%)	>8h/ night (%)	DFA	DMS	EMA	Any (%)	>1h/day (%)	Median (min) <sup>c</sup>	Median (min)	
		( )	( )								
257	420	16.0	10.5	12.5	46.1	13.4	30.5	8.2	60	426	
		17.1	7.6	13.7	39.6	13.0	22.2	5.8			
38	390	18.4	5.3	13.2	31.6	21.1	13.2	0	60	416	
88	420	20.7	9.2	18.4	47.1	11.6	21.8	9.2	60	420	
131	420	12.2	13.0	8.4	49.6	12.3	41.2	9.9	60	435	
68	420	27.9 28.4	7.4 9.8	25.4 25.3	58.8 41.9	17.9 17.2	25.0 14.2	4.4 2.4	60	420	
	257 38 88 131	N Median (min)  257 420  38 390 88 420 131 420	N Median (min) 257 420 16.0 17.1 38 390 18.4 88 420 20.7 131 420 12.2 68 420 27.9	(min)         night (%)         night (%)           257         420         16.0         10.5           17.1         7.6           38         390         18.4         5.3           88         420         20.7         9.2           131         420         12.2         13.0           68         420         27.9         7.4	N     Median   (%)   (%)     DFA	N   Median (min)   might (%) (%)   DFA   DMS	N     Median (min)     might (%)	N     Median   (%)   (%)     DFA   DMS   EMA   Any (%)	N     Median (min)   might (%)     DFA   DMS   EMA     Any (%)   > 1h/day (%)	N     Median (min)     Color     N   Median (min)     Median (min)     Median (min)     Median (min)     Median (min)     Median (min)   Me	

<sup>&</sup>lt;sup>a</sup>DFA: difficulties falling asleep; DMS: difficulties maintaining sleep; EMA: early morning arousal

**Table 3**—Age-Standardized Prevalence of Self-Perceived Poor Health Status, Depressive Mood, Regular Nocturnal Sleep Disturbances, and Excessively Short and Long Nocturnal Sleep Duration by Type of Siesta Taker Among 4,472 Subjects Without Manifest Coronary Artery Disease of the Heinz Nixdorf Recall Study, Germany, 2000-2003

	_	lar or No esta		Short iesta	·	Long esta		ort Siesta vs. r or No Siesta		ng Siesta vs. or No Siesta
Number of Men	n=1770		n=290		n=65		Standardized Prevalence Ratio (SPR)		Standardized Prevalence Ratio (SPR)	
	n	%	n	%	n	%	SPR	95%CI	SPR	95%CI
Poor Health Status	211	11.3	29	8.8	12	20.2	0.78	0.71-0.86	1.79	1.38-2.32
Depressive Mood	176	9.3	33	11.7	15	23.1	1.26	1.15-1.37	2.48	1.99-3.09
Regular DFA	118	6.2	24	8.1	7	11.5	1.31	1.16-1.49	1.85	1.17-2.95
Regular DMS	541	30.0	120	32.8	24	31.1	1.09	1.07-1.12	1.04	0.92-1.17
Regular EMA	148	7.8	21	6.4	2	4.1	0.82	0.72-0.94	0.53	0.19-1.43
Sleep duration < 6h/night	190	9.8	30	10.4	6	16.2	1.06	0.96-1.17	1.65	1.13-2.41
Sleep duration >8h/night	112	6.2	29	7.7	6	6.8	1.24	1.12-1.37	1.10	0.73-1.65
Number of Women	n=1981		n=308		n=44					
Poor Health Status	369	17.4	77	23.5	14	27.2	1.35	1.29-1.41	1.56	1.25-1.95
Depressive Mood	196	9.5	28	8.0	6	15.0	0.84	0.75-0.95	1.58	0.99-2.52
Regular DFA	219	10.4	42	12.2	12	30.4	1.17	1.09-1.27	2.92	2.25-3.80
Regular DMS	747	35.5	136	36.6	20	45.8	1.03	1.01-1.06	1.29	1.11-1.49
Regular EMA	218	10.3	56	19.6	8	23.2	1.90	1.79-2.02	2.25	1.53-3.31
Sleep duration < 6h/night	294	14.0	53	18.4	12	36.1	1.31	1.23-1.41	2.58	2.06-3.22
Sleep duration >8h/night	135	6.6	23	5.6	7	11.0	0.85	0.75-0.96	1.67	1.18-2.36

N=14 subjects were excluded because information on siesta duration was missing; poor health status: self-perceived health status rated as "less well" or "poor"; depressive mood as measured by a modified CES-D score; regular DFA: regular difficulties falling asleep; regular DMS: regular difficulties maintaining sleep; regular EMA: regular early morning awakening; SPR: Standardized prevalence ratio; ratio of age-standardized prevalences; CI: Confidence interval.

In a hypothetical follow-up study of a cohort with the risk factor distributions of the 3 siesta groups in the Heinz Nixdorf Recall Study, the estimated rate ratios for the association between baseline siesta and incident CAD are appreciably confounded

upon adjustment for few or no risk factors, among both men and women (Table 5). The adjusted estimates move closer to the hypothetically unconfounded null value upon adjustment for additional numbers of risk factors.

<sup>&</sup>lt;sup>b</sup>Overall sleep duration including sleep at night and siesta of any frequency per week

<sup>&</sup>lt;sup>c</sup>Median duration of siesta (minutes) among subjects with daily siesta

Missing data: per Item < 1%, therefore missing data were excluded.

**Table 4**—Age-Standardized Prevalence of Cardiovascular Risk Factors Stratified by Type of Siesta Taker Among 4,472 Subjects Without Manifest Coronary Artery Disease of the Heinz Nixdorf Recall Study, Germany, 2000-2003

n 794 798 463 155 977 456 682 358 642	76 76 44.9 43.3 23.5 8.5 52.1 24.4 36.7 19.3	n 207 152 67 29 155 76	290 % 71.4 43.5 25.3 7.2 51.6 22.8	n 48 33 25 12 34	<b>96</b> 73.9 34.1 41.5	SPR 1.59 1.00	95%CI 1.31-1.94		ized Prevalence tio (SPR) 95%CI 1.12-2.41
794 798 463 155 977 456 682 358 642	44.9 43.3 23.5 8.5 52.1 24.4	207 152 67 29 155 76	71.4 43.5 25.3 7.2 51.6	48 33 25 12	73.9 34.1	1.59 1.00	1.31-1.94	1.65	1.12-2.41
798 463 155 977 456 682 358 642	43.3 23.5 8.5 52.1 24.4	152 67 29 155 76	43.5 25.3 7.2 51.6	33 25 12	34.1	1.00			
463 155 977 456 682 358 642	23.5 8.5 52.1 24.4 36.7	67 29 155 76	25.3 7.2 51.6	25 12			0.00.1.02	0.70	
155 977 456 682 358 642	8.5 52.1 24.4 36.7	29 155 76	7.2 51.6	12	41.5		0.99-1.02	0.79	0.73-0.85
977 456 682 358 642	52.1 24.4 36.7	155 76	51.6			1.08	1.03-1.12	1.77	1.57-1.99
456 682 358 642	24.4 36.7	76		3.1	13.5	0.85	0.77-0.93	1.59	1.25-2.02
682 358 642	36.7		22.8	27	43.7	0.99	0.97-1.01	0.84	0.77-0.91
358 642				21	27.6	0.93	0.90-0.97	1.13	0.99-1.29
358 642									
642	193	119	35.5	33	41.5	0.97	0.94-0.99	1.13	1.04-1.23
	17.0	62	18.7	25	34.3	0.97	0.92-1.02	1.78	1.60-1.97
	37.0	138	37.9	40	48.0	1.02	1.00-1.05	1.30	1.22-1.38
74	4.3	22	6.4	10	12.0	1.49	1.28-1.73	2.79	2.15-3.62
iovascular	Risk Factor	·Sp							
155	8.3	13	5.5	1	6.2	0.66	0.54-0.81	0.75	0.10-5.38
297	16.3	46	17.3	8	16.0	1.06	1.00-1.13	0.98	0.65-1.49
382	22.0	56	21.4	10	14.3	0.97	0.92-1.02	0.65	0.49-0.87
358	20.1	73	21.7	13	19.6	1.08	1.04-1.12	0.98	0.80-1.18
234	13.6	45	15.1	8	12.1	1.11	1.04-1.18	0.89	0.66-1.20
139	8.3	27	9.0	13	16.1	1.08	0.96-1.22	1.94	1.59-2.37
60	3.6	13	3.0	5	4.9	0.83	0.68-1.03	1.36	0.85-2.18
16	1.0	1	0.2	2	2.7	0.20	0.05-0.84	2.70	0.69-10.53
2	0.1	1	0.2	2	1.2	2.00	0.05-74.83	12.00	1.11-129.41
0		0		0					
n=1	1981	n=	308	n=	=44				
n	%	n	%	N	%				
918	46.3	223	72.4	32	72.7	1.56	1.29-1.89	1.57	0.99-2.49
588	28.3	113	29.0	15	28.2	1.02	1.00-1.05	1.00	0.81-1.22
438	19.8	50	19.1	11	29.3	0.96	0.91-1.03	1.48	1.20-1.82
118	5.8	16	3.6	8	17.8	0.62	0.53-0.72	3.07	2.18-4.33
994	47.8	167	43.8	29	57.0	0.92	0.90-0.93	1.19	1.07-1.32
540	25.9	93	25.7	17	34.5	0.99	0.96-1.03	1.33	1.10-1.61
898	43.1	164	43.7	27	55.3	1.01	0.99-1.04	1.28	1.15-1.44
446	21.3	69	17.1	10	21.2	0.80	0.77-0.83	1.00	0.77-1.29
271	13.9	63	13.2	8	12.8	0.95	0.91-0.99	0.92	0.63-1.35
90	4.5	19	4.9	2	2.2	1.09	В-94-1.27	0.49	0.17-1.42
			161		2.5	1.00		0.27	0.04.1.01
									0.04-1.81
									0.86-1.43
									0.56-1.23
									0.81-1.73
									0.52-1.36
									1.10-2.82
					8.5			4.05	1.72-9.55
	0.2	1	0.3	0		1.50	0.10-22.17		
	155 297 382 358 234 139 60 16 2 0 <b>n</b> =1 <b>n</b> 918 588 438 118 994 540	155 8.3 297 16.3 382 22.0 358 20.1 234 13.6 139 8.3 60 3.6 16 1.0 2 0.1 0	297 16.3 46 382 22.0 56 358 20.1 73 234 13.6 45 139 8.3 27 60 3.6 13 16 1.0 1 2 0.1 1 0	155 8.3 13 5.5 297 16.3 46 17.3 382 22.0 56 21.4 358 20.1 73 21.7 234 13.6 45 15.1 139 8.3 27 9.0 60 3.6 13 3.0 16 1.0 1 0.2 2 0.1 1 0.2 0 0	155 8.3 13 5.5 1 297 16.3 46 17.3 8 382 22.0 56 21.4 10 358 20.1 73 21.7 13 234 13.6 45 15.1 8 139 8.3 27 9.0 13 60 3.6 13 3.0 5 16 1.0 1 0.2 2 2 0.1 1 0.2 2 0 0 0 0   n=1981	155   8.3   13   5.5   1   6.2	155   8.3   13   5.5   1   6.2   0.66	155   8.3   13   5.5   1   6.2   0.66   0.54-0.81	155   8.3

N=14 subjects were excluded because information on siesta duration was missing; poor health status: self-perceived health status rated as "less well" or "poor"; depressive mood as measured by a modified CES-D score; regular DFA: regular difficulties falling asleep; regular DMS: regular difficulties maintaining sleep; regular EMA: regular early morning awakening; SPR: Standardized prevalence ratio; ratio of age-standardized prevalences.

 $<sup>^{\</sup>rm a}$  prevalences of age  $\geq$  60 years are crude prevalences; prevalence ratio of crude prevalences.

<sup>&</sup>lt;sup>b</sup> due to missing data of either of the 9 modifiable risk factor, the overall N of male irregular or no siesta takers is 1643, of daily short takers is 275 and of daily long takers is 62.

<sup>&</sup>lt;sup>c</sup> due to missing data of either of the 9 modifiable risk factor, the overall N of female irregular or no siesta takers is 1860, of daily short takers is 289 and of daily long takers is 41.

**Table 5**—Hypothetical Coronary Artery Disease Rate Ratio Estimates Adjusted for Varying Numbers of CAD Risk Factors in a Hypothetical Cohort with Risk Factor Distributions Like Those Of The Siesta Groups in the Heinz Nixdorf Recall Study

Assumed rate ratio for each risk factor <sup>a</sup>	Adjustment set		Estimated 10-year Rate Ratios of Coronary Artery Disease					
Men		No/irregular siesta	Daily Short siesta	Daily Long siesta				
1.3	None	Reference Group	1.14	1.45				
	Age	Reference Group	1.00	1.17				
	Age & smoking	Reference Group	0.99	1.09				
	Age, smoking & diabetes	Reference Group	1.00	1.08				
	Age, smoking, diabetes & hypertension	Reference Group	1.02	1.10				
	Age, smoking, diabetes, hypertension & waist	Reference Group	1.01	1.10				
1.5	None	Reference Group	1.20	1.76				
	Age	Reference Group	1.00	1.28				
	Age & smoking	Reference Group	0.98	1.16				
	Age, smoking & diabetes	Reference Group	1.00	1.14				
	Age, smoking, diabetes & hypertension	Reference Group	1.03	1.18				
	Age, smoking, diabetes, hypertension & waist	Reference Group	1.01	1.17				
1.7	None	Reference Group	1.24	1.98				
	Age	Reference Group	0.99	1.38				
	Age & smoking	Reference Group	0.97	1.22				
	Age, smoking & diabetes	Reference Group	1.00	1.20				
	Age, smoking, diabetes & hypertension	Reference Group	1.04	1.24				
	Age, smoking, diabetes, hypertension & waist	Reference Group	1.00	1.23				
2.0	None	Reference Group	1.29	2.06				
	Age	Reference Group	0.99	1.43				
	Age & smoking	Reference Group	0.96	1.27				
	Age, smoking & diabetes	Reference Group	0.99	1.25				
	Age, smoking, diabetes & hypertension	Reference Group	1.04	1.33				
	Age, smoking, diabetes, hypertension & waist	Reference Group	1.00	1.32				
Women								
1.3	None	Reference Group	1.13	1.28				
	Age	Reference Group	0.98	1.16				
	Age & smoking	Reference Group	0.98	1.20				
	Age, smoking & diabetes	Reference Group	0.99	0.98				
	Age, smoking, diabetes & hypertension	Reference Group	0.98	0.99				
	Age, smoking, diabetes, hypertension & waist	Reference Group	0.97	0.98				
1.5	None	Reference Group	1.20	1.43				
	Age	Reference Group	0.96	1.26				
	Age & smoking	Reference Group	0.96	1.36				
	Age, smoking & diabetes	Reference Group	0.97	0.97				
	Age, smoking, diabetes & hypertension	Reference Group	0.96	0.98				
	Age, smoking, diabetes, hypertension & waist	Reference Group	0.95	0.96				
1.7	None	Reference Group	1.25	1.57				
	Age	Reference Group	0.95	1.35				
	Age & smoking	Reference Group	0.94	1.50				
	Age, smoking & diabetes	Reference Group	0.96	0.96				
	Age, smoking, diabetes & hypertension	Reference Group	0.95	0.96				
	Age, smoking, diabetes, hypertension & waist	Reference Group	0.93	0.93				
2.0	None	Reference Group	1.30	1.72				
	Age	Reference Group	0.94	1.46				
	Age & smoking	Reference Group	0.92	1.65				
	Age, smoking & diabetes	Reference Group	0.94	0.95				
			0.00	0.04				
	Age, smoking, diabetes & hypertension	Reference Group	0.92	0.94				

<sup>&</sup>lt;sup>a</sup> Risk factors adjusted for were: age, smoking, diabetes, hypertension, dyslipidemia, obesity, waist, CRP, Agatston score, ABI; all risk factors are treated as dichotomous variables; we assumed that siesta has no effect on the CAD incidence

#### **DISCUSSION**

In our sample, the small number of participants who took daily long siestas were older, disproportionately male, and had a relatively high prevalence of manifest CAD, depressed mood, and low self-perceived health status in comparison with those who took shorter siestas and with those who took siestas irregularly or never. In the subset of participants lacking manifest CAD at baseline, the taking of daily long siestas was associated with increased prevalence of most CAD risk factors and with unfavorable distributions of 2 subclinical CAD measures: ABI and coronary calcium score. These results corroborate recent epidemiologic findings in Costa Rica and Israel<sup>4,27</sup> that daily takers of relatively long siestas constitute a highrisk group. It is unclear whether these findings contradict the Greek case-control studies, because regularity of midday napping was not reported in those studies.<sup>2,3</sup>

Naska et al<sup>7</sup> studied the association between siesta and coronary mortality in a population-based study in Greece among 17,086 men and 23,380 women, aged 20-86 years. Although the investigators assessed the mean siesta duration, they did not report the association between long regular siestas and coronary mortality. It has been hypothesized that long siestas are associated with increased risk of cardiovascular mortality and incident myocardial infarction. Several factors hamper a comparison of our results with those from Naska et al. They excluded patients with histories of cancer or angina, used a different definition of regular siestas, and adjusted for 3 additional variables (physical activity, Mediterranean diet score, and employment status).

The prevalence of regular siesta in our study was considerably lower than in studies that investigated the association between siesta habits and coronary heart disease in Costa Rica and Israel. In Costa Rica, for example, Burazeri et al reported a prevalence of regular siestas of 41% among men and 33% among women. Among persons of similar age in our study, the prevalence was 16% in both sexes.<sup>6</sup> The prevalence of taking siestas at least once per week was 70% in Costa Rica (control group) and 51% in our study among subjects without manifest CAD.<sup>4</sup> A higher prevalence of siesta-taking among participants with manifest CAD has also been observed by others.<sup>5,6,27</sup> This may indicate, at least in part, that siesta is a consequence of CAD, for the simple reason that persons with CAD may be sick and tired.

Those who take daily, long siestas are of concern not only clinically, but with regard to potential confounding in studies of siestataking in relation to incident cardiovascular outcomes. Burazeri et al<sup>6</sup> observed increased cardiovascular mortality among men, but not women, who took daily siestas of very long duration (at least 2 hours per day). There were not enough participants in our study who took daily siestas of this length to support a meaningful analysis. Nevertheless, though Burazeri et al adjusted for some cardiovascular risk factors, our sensitivity analyses suggest that residual confounding by additional risk factors might have contributed appreciably not only to that association, but to associations in studies in which the takers of daily, long siestas were grouped with those taking less regular siestas, shorter siestas, or both.<sup>5</sup>

The finding that one CAD risk factor, hypertension, is inversely associated with the taking of daily, long siestas at baseline among men in our cohort indicates that the confounding of associations between siesta and cardiovascular outcomes is not of necessity upward. The magnitude and even the direction of the net confounding by unmeasured, poorly measured, or incompletely specified CAD

risk factors may vary from place to place and from time to time. Thus, we recommend that sensitivity analyses of uncontrolled confounding<sup>31,32</sup> be conducted for all previous studies of this topic as well as future studies. The best time to conduct these sensitivity analyses would be before collecting any data, in the design phase of a study, to guide the breadth and depth of data collection on potential confounders. The simple assumptions of the same rate ratio for each risk factor and of a multiplicative relation among multiple risk factors in our sensitivity analyses could be replaced by evidence-based estimates from systematic literature reviews of the specific unmeasured risk factors of concern in a given study.

Additional studies on siesta habits in relation to measures of subclinical atherosclerosis are needed to compare with our results. The adverse distributions of coronary calcium and ABI we observed among men taking daily long siestas suggest that the atherosclerotic burden is particularly high in this group.

Of equal importance to the potential identification of takers of daily long siestas as a special high-risk group is the implication that persons taking daily siestas of shorter duration do not stand out in our results. In every analysis, this group was more similar to those who took no siestas or who took siestas irregularly than to the special group who took daily long siestas. The extent to which this result might be generalizable to other populations is unknown and should be determined in studies of populations in different climates and cultures, including reanalyses of existing data.

There is evidence from several prospective cohort studies that depression is a risk factor for CAD.33 Depressed mood was positively associated with siesta-taking in our cross-sectional data. Thus, confounding by depression may further complicate the study of the association between siesta-taking and cardiovascular disease incidence. Ohayon et al found that severe daytime sleepiness, which is not necessarily a surrogate for daily siesta-taking, was associated with prevalence of depressive disorder.<sup>34</sup> To our knowledge, none of the prospective studies on siesta and cardiovascular disease incidence or mortality have adjusted for depressed mood. The relationship is further complicated by the fact that sleep problems can contribute to the diagnosis of depressive disorder. Our approach to this problem was to remove the sleep item from the depressive symptom scale we used. This strategy may not always be possible (e.g., with clinically diagnosed major depressive disorder).

Self-perceived poor health is a correlate of nocturnal sleep disturbances.<sup>35-37</sup> Like Burazeri et al,<sup>6</sup> we found that self-perceived poor health is associated with daily siestas of long duration. This result further supports the view that it may not be siesta itself but cardiovascular risk factors, subclinical atherosclerosis, and other diseases that explain higher observed cardiovascular risks among daily takers of long siestas. The observation of Bursztyn et al that not only increased cardiovascular disease mortality, but increased mortality from non-malignant, non-cardiovascular diseases as well, corroborates this hypothesis.<sup>5</sup>

We found evidence of little or no association between the frequency of nocturnal sleep disturbances (difficulties falling asleep, maintaining asleep, early morning arousal) and siesta frequency. We found that daily short and long siestas were associated with regular difficulties falling asleep at night, suggesting that the taking of daily siestas might represent compensation for poor nocturnal sleep quality. Bursztyn et al found that siesta-taking was associated with increased nocturnal sleep satisfaction,<sup>5</sup> but they did not specifically examine daily long siestas separately.

There are several factors that limit our results. First, the information on sleep habits came from self-reports and was not validated. Second, the interview questions did not draw a distinction between voluntary and involuntary afternoon naps (i.e., falling asleep while intending to remain awake). In addition, we did not ask for the context in which napping is most common, such as the typical time during the day for napping, nap environment (e.g., light and noise level), mode of awakening, sleepiness after awakening, and sleep satisfaction. Third, obesity, snoring, and daytime sleepiness have been reported to be key markers of sleep apnea, 38-40 which is plausibly associated with siesta-taking. We were unable to assess the association between obstructive sleep apnea and siesta-taking because we did not collect information on snoring and sleep apnea. The weak association between siesta-taking and obesity may reflect at least some of the consequences of sleep apnea.

In conclusion, daily long siestas are associated with poor selfperceived health status, depressive mood, and regular difficulties falling asleep among men and women in this cross-sectional sample. Daily long siestas are associated with excessively short and long sleep durations and with early morning awakening among women. Daily long siestas are also associated with several cardiovascular risk factors and with measures of subclinical atherosclerosis among men and women. These associations may complicate prospective studies of siesta-taking in relation to incident cardiovascular disease by creating confounding, which our sensitivity analyses suggest may be difficult to control adequately. Daily short siestas and irregular siestas were not strongly associated with increased prevalence of cardiovascular risk factors, subclinical atherosclerosis, or sleep disturbances in our study. The taking of infrequent or relatively short siestas, therefore, may not be indicative of preclinical cardiovascular disease or of risk factor clustering and may thus be innocuous.

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